Chapter 8
Antibiotics Use in African Aquaculture: Their Potential Risks on Fish and Human Health

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8.1 Introduction

It is globally undoubtedly accepted that antibiotics have saved many lives and eased the suffering of many millions of animals (Byarugaba 2004). However, antibiotics, of either natural or synthetic origin, are used abusively in human, livestock, agriculture, and aquaculture both to prevent proliferation and destroy bacteria (Mehdi et al. 2018). Consequently, antibiotics exist ubiquitously in the environment and are currently deemed as a global pandemic problem posing a health risk to aquatic animals and humans. Unfortunately, the risks caused by antibiotics globally are expected to continue because, between 2000 and 2015 their consumption increased 65% from 21.1 to 34.8 billion defined daily doses (DDDs), and the antibiotic consumption rate increased 39% from 11.3 to 15.7 DDDs per 1000 inhabitants per day (Klein et al. 2018). Astonishingly, the increase in consumption of antibiotics was driven by low- and middle-income countries (LMICs), a characteristic possessed by the majority of African countries.

The African continent poses peculiar features regarding antibiotics consumption. First, most African countries are generally characterized by poverty, ignorance, poor sanitation, hunger and malnutrition, poor and inadequate health care systems, civil conflicts and bad governance (Byarugaba 2004), coupled with an inappropriate prescription as well as self-medication and free sale of antibiotics (Sanou et al. 2018). Secondly, most African countries have weak regulatory agencies and absence/weak regulations concerning antibiotics usage. Accordingly, antibiotics are indiscriminately given as over-the-counter drugs at community pharmacies

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A. L. K. Abia, G. R. Lanza (eds.), *Current Microbiological Research in Africa*,
https://doi.org/10.1007/978-3-030-35296-7_8

(Mukonzo et al. 2013), which have been strongly correlated with antibiotic-resistant bacteria (ARB) and antibiotics resistance genes (ARGs) in aquatic animals such as fish and humans in LMICs (Alsan et al. 2015). The lack of regulatory agencies in African countries have caused the indiscriminate use of antibiotics in human for disease treatments and as therapeutic and growth promoters in livestock, agriculture, and aquaculture production. As growth promoters, antibiotics are believed to improve feed conversion, promote animal growth, and reduce mortality and morbidity rates resulting from clinical and subclinical illnesses (Foka et al. 2018).

Moreover, antibiotics applied in fish are poorly absorbed in the intestine, and subsequently are released into the aquatic environments where they selectively cause ARB and ARGs (Fu et al. 2017). Thus, antibiotic resistance in bacteria and genes that cause diseases in man is an issue of significant concern, which is expected to become the leading global cause of death by 2050 (O'Neill 2016). Although the misuse of antibiotics in human medicine is the principal cause of ARB and ARBs in Africa, the use of antibiotics in food animals and their subsequent release into the aquatic environments are contributory factors (Barton 2000; Goutard et al. 2017; Adegoke et al. 2018). Apart from ARB and ARGs, antibiotics also cause human health risk due to their residue amounts in various contaminated foods consumed in Africa (Darwish et al. 2013).

The increasing human population in Africa has led to an increase in reliance on aquaculture to supply safe, reliable, and economical food, contributing 10% of the total global population engaged in fisheries and aquaculture, second only to Asia with 84% (FAO 2018). In some African countries such as Ghana and Sierra Leone, fish contributes or exceeds, 50% of total animal protein intake (FAO 2016). Aquaculture production, mainly from catfish and tilapia, accounted for 17–18% of total fish production in Africa (Fig. 8.1), with a general increasing trend (Fig. 8.2) (FAO 2018). The per capita fish food consumption for Africa was reported as 9.9 kg/year in 2015, partly contributed by unreported data (FAO 2018).

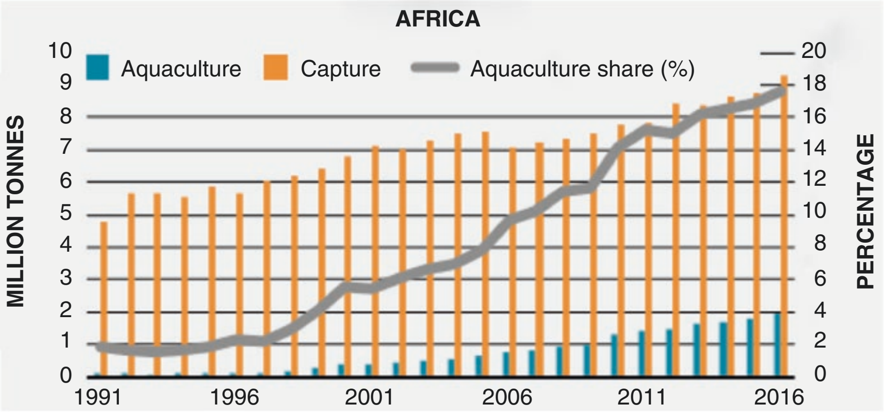

Fig. 8.1 Aquaculture contribution to total fish production (excluding aquatic plants). Source: FAO (2018)

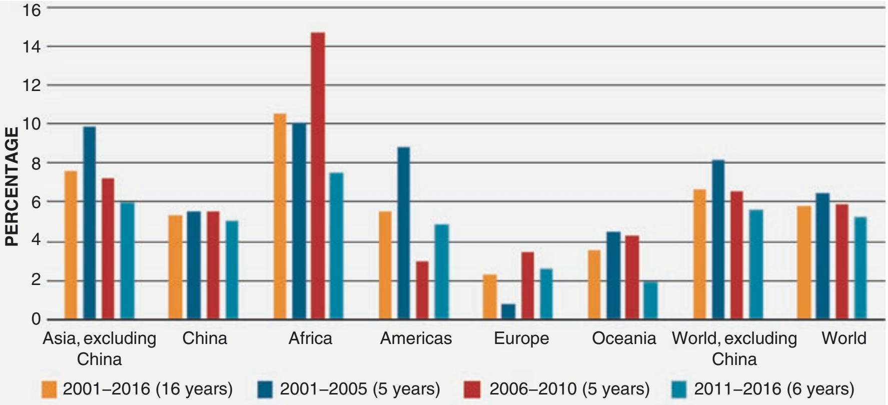

Fig. 8.2 Average annual growth rate of aquaculture production by volume (excluding aquatic plants). Source: FAO (2018)

Although the available information suggests minimal use of antibiotics in aquaculture in African countries, potential contamination of fish from fertilizers used in animals treated with antibiotics is unavoidable (Shah et al. 2012; Wamala et al. 2018), because most farmers fertilize their ponds. However, the effects of antibiotics on fish anatomy and physiology from an African perspective are currently poorly understood, and information on ARB and ARGs in fish and humans due to fish exposure is currently scattered and unfocused. Furthermore, antibiotics are increasingly used in humans and other food animals, with a concomitant prevalence of ARB and ARGs in LMICs (Bernabé et al. 2017). It has been shown that infections caused by ARB may increase health care costs due to patients' need for more diagnostic tests, more extended hospitalization periods, and poor treatment outcomes (Nyasulu et al. 2012). Despite all these, little attention has been directed towards understanding the antibiotics residues in fish, other food animals, and humans in Africa (Adegoke et al. 2018).

For the first time, this chapter organizes and synthesizes the available information in the literature on the potential risks of antibiotics on cultured fish and human health from Africa. The chapter assesses the effects of antibiotics on fish growth performance, feed utilization, hepatotoxicity and nephrotoxicity, and hematological parameters. It further evaluates the potential human health risks caused by the existence of ARB and ARGs in fish and other consumed foods, in addition to direct risks due to the consumption of fish products containing antibiotics residues. The information generated informs policies to limit the use of antibiotics in food animals by enforcing policies, which regulate their use in Africa to safeguard human health.

8.2 Effects of Antibiotics on Growth Performance and Feed Utilization

Growth performance, feed utilization, survival rate, and body development are important production attributes to fish growers because they affect directly the yield and economics of an aquaculture enterprise. Thus, understanding the effects of antibiotics on these aspects in cultured fish deserves a peculiar consideration. In Africa, very few studies have currently used antibiotics to study growth and related parameters on fish. The literature visited indicated oxytetracycline studied in *O. niloticus* (El-Sayed et al. 2014), oxytetracycline and florfenicol in *O. niloticus* ♀ × *O. aureus* ♂ hybrids (Reda et al. 2013), and chloramphenicol researched in *O. niloticus* (Shalaby et al. 2006) and African catfish, *Clarias gariepinus* (Nwani et al. 2014) were the only antibiotics used. Results from these few studies indicated improved growth of treated fish compared to controls. For example, the growth performance of *O. niloticus* increased significantly with increasing levels of chloramphenicol (Shalaby et al. 2006). Moreover, feeding diets containing oxytetracycline and florfenicol in *O. niloticus* ♀ × *O. aureus* ♂ hybrids (Reda et al. 2013) and *O. niloticus* (El-Sayed et al. 2014) resulted into faster growth performance in treated than control fish.

The precise reasons for the enhanced growth performance of fish after antibiotics administration are subject to scrutiny. Increased growth has been attributed to higher feed consumption and reduced feed conversion ratio. Indeed, the growth rate was increased in *O. niloticus* treated with chloramphenicol (Shalaby et al. 2006), oxytetracycline and florfenicol (Reda et al. 2013), and oxytetracycline (El-Sayed et al. 2014), in which feed consumption and intake were increased, while feed conversion ratio was reduced. Moreover, apparent protein, lipid, carbohydrate, and energy digestibility were increased in *O. niloticus* fed on chloramphenicol (Shalaby et al. 2006). These results should be interpreted with caution due to limited studies and the existence of contradicting results elsewhere. It has been recently shown that antibiotics, particularly oxytetracycline, do not cause growth promotion in finfish (Trushenski et al. 2018) and causes multiple effects in Nile tilapia including reduced nutrients digestibility and digestive enzymes (Limbu et al. 2018), growth performance (Limbu et al. 2019a; Limbu et al. (2019b), protein and feed efficiencies (Limbu et al. 2019b).

Like growth performance, studies conducted on the effects of antibiotics on survival rate are also limited. The results obtained in the limited studies do not show any influence of antibiotics on fish survival rate. Exposure to dietary oxytetracycline (El-Sayed et al. 2014) and chloramphenicol (Shalaby et al. 2006) both in *O. niloticus* and chloramphenicol in *C. gariepinus* (Nwani et al. 2014) did not significantly influence survival rate of treated fish relative to control. Results detailing the effects of antibiotics on body development are based on *C. gariepinus* exposed to chloramphenicol baths (Nwani et al. 2014). In this study, treated fish had abnormal behavioral changes at higher concentration of chloramphenicol. The fish swam near the water surface, lost equilibrium, swam erratically, had hyperactivity, and stayed motionless on the bottom of the culture tank. Furthermore, exposed fish had clinical toxic signs such as lightening in skin color of the body surface, erosion of fins and tails, and increased mucus secretions from the whole body. These results indicate that antibiotics application on fish leads to body malformation and damage, which may lead to physiological and metabolic dysfunctions affecting fish health.

8.3 Effects of Antibiotics on Fish Health

8.3.1 Oxidative Stress, Hepatotoxicity, and Nephrotoxicity

Antibiotics used in fish production induce oxidative stress, which affects antioxidant enzymes that protect fish body from reactive oxygen species (ROS) (Limbu et al. 2018). Changes in the activities of antioxidant enzymes indicate an imbalance in the ROS production in the body. Limited studies have been conducted in Africa to assess the antioxidant capacity of fish exposed to antibiotics. A study conducted by Olaniran et al. (2018) indicated reduced glutathione S transferase (GST) and superoxide dismutase (SOD) activities in *C. gariepinus* exposed to tetracycline. The decreased antioxidants in fish treated with antibiotics may be caused by an excess accumulation of free radicals, such as superoxide anion and hydrogen peroxide beyond the antioxidant capacity to counteract (Yonar et al. 2011; Yonar 2012; Oliveira et al. 2013; Wang et al. 2014). This may oxidize amino acids and cofactors, which may affect the general fish health. Malondialdehyde (MDA) is the main oxidative product of peroxidized polyunsaturated fatty acids and is an important index of lipid peroxidation. The extent of lipid peroxidation is measured in tissues by quantification of thiobarbituric acid reactive substances (TBARS) expressed as MDA concentration (Nunes et al. 2015). Lipid peroxidation is the initial step of cellular membrane damage caused by xenobiotics such antibiotics (Yonar et al. 2011; Yonar 2012). Limited studies have reported on lipid peroxidation using MDA. Reduced MDA level was reported in *C. gariepinus* exposed to tetracycline, indicating lack of lipid peroxidation (Olaniran et al. 2018).

The liver of fish and other vertebrates is known for its digestive, metabolism, storage, and detoxification functions. The introduction of antibiotics in fish body through medicated feeds may cause liver damage effects that might impair its functions (Dobšíková et al. 2013). Limited studies have reported on the effects of antibiotics on the hepatosomatic index (HSI) as an indicator of hepatotoxicity in fish. The chloramphenicol medicated feeds used in *O. niloticus* did not cause significant variations in HSI in experimental compared to control fish (Shalaby et al. 2006). Few studies conducted limit the ability to draw logical conclusions. Studies conducted in other parts of the world showed HSI was reduced (Refstie et al. 2006; Limbu et al. 2018) and increased (Topic Popovic et al. 2012; Nakano et al. 2018; Trushenski et al. 2018) in different fish species.

The amount of circulating proteins reflects an organism's physiology. Plasma proteins and glucose in the circulatory system transport lipids, hormones, vitamins, and minerals and regulate cellular activities, functioning of the immune system, and blood clotting. Imbalances in the plasma protein and glucose counts indicate liver damage, which interferes with its normal functions. A dose-dependent increase in plasma protein levels was reported in *O. niloticus* exposed to chloramphenicol diet, indicating osmoregulatory dysfunction, hemodilution, or tissue damage surrounding blood vessels (Shalaby et al. 2006). Moreover, plasma glucose increased significantly with increasing levels of chloramphenicol (Shalaby et al. 2006). Although limited, this study indicated that antibiotic medications in cultured fish lead to disturbances in plasma proteins and glucose, which indicate hepatotoxicity.

Except for plasma proteins and glucose, liver dysfunction is manifested by increased levels of specific serum enzymes activities, which signal cellular leakage and impaired liver cell membrane integrity and function. Alanine transaminase (ALT) and aspartate aminotransaminase (AST) are required in the metabolism of amino acids, and their change in activities reflect their leakage into the blood after cytolysis in the liver (Han et al. 2014). Thus, AST and ALT enzymes are commonly used to detect hepatotoxicity due to xenobiotics exposure (Saravanan et al. 2012). Studies from Africa assessing liver damage in cultured fish after antibiotics by using AST and ALT have reported contrasting results. The administration of florfenicol diet in *O. niloticus* did not alter ALT activity (Reda et al. 2013).

On the contrary, the activities of AST and ALT in plasma decreased significantly with increasing levels of dietary chloramphenicol in *O. niloticus* (Shalaby et al. 2006). The observed decrease in AST and ALT activities in fish is either due to insufficient detoxification mechanisms to prevent the toxicity action of antibiotics on these enzymes or failure of liver damaged cells to synthesize AST and ALT proteins (Saravanan et al. 2012). On the other hand, oxytetracycline-supplemented diets increased significantly ALT activity in *O. niloticus* (Reda et al. 2013). Increased ALT activity is due to the ability of antibiotics to accumulate or bind to different cells leading to damage and disintegration of cells, releasing ALT into blood circulation, suggesting impaired liver function.

Histopathological effects provide a quick diagnosis to detect abnormalities in various fish tissues and organs after antibiotics exposure. Antibiotics use indicate species- and antibiotic-specific histopathological effects in the liver and kidney of treated fish. Feeding dietary oxytetracycline and florfenicol in *O. niloticus* (Reda et al. 2013) induced various pathological alterations in liver and kidney of treated fish. Moreover, both dietary oxytetracycline and florfenicol decreased creatinine in the treated *O. niloticus* than the control fish (Reda et al. 2013). The existence of several histopathological damages in the liver of treated fish is due to liver degenerations (Reda et al. 2013) and inhibition of somatic cells in mitochondrial protein synthesis by antibiotics resulting in lack of oxidative ATP-generating capacity, which causes proliferation arrest of normal and malignant epithelial cells (Bakke-McKellep et al. 2007). These changes induce hepatotoxicity and nephrotoxicity.

8.3.2 Effects of Antibiotics on Hematological Parameters

Hematological parameters provide essential information on the health of cultured fish after antibiotics application. Results conducted in hematological parameters are still contrasting. Dietary chloramphenicol exposure did not affect mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) in *O. niloticus* (Shalaby et al. 2006) and monocytes, eosinophils, and basophils in *C. gariepinus* (Nwani et al. 2014). Moreover, florfenicol did not show significant differences in immunoglobulin M (IgM) total levels and phagocytic activity in *O. niloticus* when compared to the control fish (Reda et al. 2013).

However, a concentration- and time-dependent decrease in hemoglobin (Hb), red blood cells (RBC) counts, and MCV were detected in *C. gariepinus* exposed to chloramphenicol bath (Nwani et al. 2014). The different toxic effects of chloramphenicol bath on various organs caused the observed decrease in Hb, RBC, and MCV in fish. Chloramphenicol suppressed the production of hematological parameters caused by their toxic accumulation in lymphoid organs and pronephros (Nwani et al. 2014). The decreased RBC counts after exposure to antibiotics is due to swelling of RBC, the release of immature erythrocytes, anemia caused by tissues damage, damaged RBC, decrease in erythrocyte life span, and suppressive effects of antibiotics on erythropoietic tissues (Shalaby et al. 2006; Nwani et al. 2014). The deecreased Hb may limit the oxygen-carrying capacity of the fish blood (Nwani et al. 2014) and affect their survival rate. The inhibition of these hematological parameters may lead to sustained toxic effects caused by both dietary and bath exposure to antibiotics, resulting in tissue damage and immunity suppression with possible fatal outcomes.

Notwithstanding the above results, dietary chloramphenicol exposure in *O. niloticus* increased RBC, Hb, and hematocrit (Shalaby et al. 2006) and its bath elevated WBC, neutrophil count, and lymphocytes in *C. gariepinus* (Nwani et al. 2014). The use of oxytetracycline diet increased lysozyme activity in *O. niloticus* (Reda et al. 2013). Increased WBC count and lysozyme activity indicate a protective mechanism of the fish body to antibiotics-induced stress, a condition termed as leukocytosis, which signals a response of damaged tissues and immune system stimulation to counteract antibiotics toxicity (Ambili et al. 2013). An increase in RBC is due to a compensation mechanism for impaired oxygen uptake caused by tissue damages due to the presence of antibiotics in the fish body and high percentage of circulating immature RBC (Ambili et al. 2013). On the other hand, the increased lymphocyte count (lymphocytosis) and the formation of blood cellular components (hematopoiesis) are features of infection due to increased disease-fighting cells after antibiotics exposure in fish. In general, dietary and bath antibiotics exposure in cultured fish cause leukocytosis, hematopoiesis, and lymphocytosis, suggesting sustained toxic effects and compensatory responses to conciliate the fish body to normal health conditions.

8.4 Potential Human Health Risks from Consumption of Antibiotics-Cultured Fish

8.4.1 Antibiotic-Resistant Bacteria and Antibiotic Resistance Genes

The widespread and indiscriminate use of antibiotics in different environmental compartments including fish, agriculture, and human health have led to the development of ARB, ARGs, and transposons. Resistant bacteria and resistance genes may be horizontally or vertically transferred among bacterial communities, the environment, and finally human being via transposons (Biyela et al. 2004). The presence of ARB and ARGs in humans affects the ability of antibiotics to treat diseases and thus compromise their health. Thus, presently, the existence of ARB and ARGs in the environments, particularly those conferring resistance to antibiotics used to treat human diseases, is an issue of major global concern. Although the misuse of antibiotics in human medicine is the principal cause of the problem, ARB and ARGs originating from animals such as fish and agriculture production are also responsible (Barton 2000).

The literature shows that ARB and ARGs pose a human health risk in various African countries contributed by consuming contaminated fish, shrimp, vegetables, and various food sources as well as drinking contaminated water (Table 8.1). The human health risk posed by ARB from fish consumption appears to be widely spread because both cultured and wild fish have been shown to contain them. Various ARB have been isolated in cultured fish from Ghana (Agoba et al. 2017), Tanzania (Shah et al. 2012; Mhongole et al. 2017), and Uganda (Bosco et al. 2012; Wamala et al. 2018). Moreover, wild fish from Uganda (Wamala et al. 2018), Algeria (Dib et al. 2018), South Africa (Fri et al. 2018), and Egypt (Ramadan et al. 2018) were all shown to contain ARB. The ARB contained in fish in the different countries originate from various sources including animal-origin fertilizers (Shah et al. 2012; Omojowo and Omojasola 2013), the aquatic environment (Stenstrom et al. 2016), and possibly fish feeds. It is possible that the ARB from the different compartments are transferred to humans in Africa. Indeed, ARB have been detected in humans from Ethiopia (Kibret and Abera 2014), Ghana (Obeng-Nkrumah et al. 2013), Ivory Coast (Moroh et al. 2014), Libya (Mohammed et al. 2016), and Morocco (El Bouamri et al. 2015). This is an alarming situation because most of the bacteria isolated exhibited high resistance to common antibiotics used for treating frequently occurring diseases in humans in Africa and most of them had multiple antibiotic resistance (MAR) (Bosco et al. 2012; Omojowo and Omojasola 2013; Mohammed et al. 2016; Agoba et al. 2017; Apenteng et al. 2017; Wamala et al. 2018). Although correct and appropriate food cooking procedures may kill bacteria, contamination can occur through improper handling before cooking (Darwish et al. 2013) and possibly through bacteria-human contact because ARB are ubiquitous (Mhongole et al. 2017). Indeed, high levels of antimicrobial resistance (AMR) were obtained in food

Table 8.1 Antibiotic-resistant bacteria isolated from fish and other environments in Africa

Resistant bacterial strain	Resistance to antibiotic	Sample isolated	Country	Reference
Most isolated bacteria (≥70%)	Penicillin, ampicillin, flucloxacillin, and tetracycline	Catfish and tilapia farms	Ghana	Agoba et al. (2017)
10% of isolates	Resistant to all the nine tested antimicrobials (MAR)	Water, sediments, and fishpond	Tanzania	Shah et al. (2012)
Pseudomonas aeruginosa	77.78% were MAR	Fish ponds	Ghana	Apenteng et al. (2017)
Salmonella typhi	70% were MAR			
Escherichia coli	66.67% Resistance to more than two classes			
Salmonella spp.	82.7% Resistant to trimethoprim sulfamethoxazole	Human	Uganda	Bosco et al. (2012)
	85.3% resistant to trimethoprim-sulfamethoxazole	Animal-food origin		
Salmonella spp.	94% Sulfamethoxazole, 61% streptomycin, 22% tetracycline, 17% ciprofloxacin and nalidixic acid, 11% trimethoprim, and 6% gentamycin and chloramphenicol	Fish from pond and wastewater	Tanzania	Mhongole et al. (2017)
Aeromonas spp.	100% Penicillin and ampicillin and 23.2% cefotaxime	Fish from pond and water from wild	Uganda	Wamala et al. (2018)
Plesiomonas shigelloides	100% Penicillin and oxacillin			
Escherichia coli	100% Ampicillin, amoxicillin, cephalothin, amikacin, kanamycin, gentamicin, neomycin, and tobramycin	Wild fish and shrimp	Algeria	Dib et al. (2018)
Vibrio spp.	76.2% Amoxicillin, 67.5% ampicillin, 38.3% erythromycin, and 35.0% doxycycline	Wild fish and water from fish farms	South Africa	Fri et al. (2018)
Aeromonas hydrophila	100% Cefoxitin, 84% ampicillin, 56% ceftazidime, and 40% cefotaxime	Fish from market	Egypt	Ramadan et al. (2018)
Escherichia coli, Aeromonas hydrophila, Salmonella typhi, Staphylococcus aureus, and *Shigella dysenteriae*	100% Tetracycline, 85.6% ampicillin, 83.3% amoxicillin, 47.6% gentamicin, 66% chloramphenicol, 44.4% erythromycin, and 18.3% nalidixic acid	Cow dung fertilizer for fishponds	Nigeria	Omojowo and Omojasola (2013)

(continued)

Table 8.1 (continued)

Resistant bacterial strain	Resistance to antibiotic	Sample isolated	Country	Reference
Acinetobacter spp.	30–100% Penicillin G, ceftriaxone, nitrofurantoin, erythromycin, and augmentin, 10% oxytetracycline, and 9% minocycline	Freshwater and soil samples	South Africa	Stenstrom et al. (2016)
Escherichia coli, *Klebsiella* spp., and *Proteus* spp.	85.6% Erythromycin, 88.9% amoxycillin, and 76.7% tetracycline	Human	Ethiopia	Kibret and Abera (2014)
ESBL producers	92.6% Cotrimoxazole, 91.2% gentamicin, 44.8% amikacin, and 41.1% ciprofloxacin	Human	Ghana	Obeng-Nkrumah et al. (2013)
Escherichia coli, *Staphylococcus aureus*, *Klebsiella pneumoniae,* and *Enterobacter aerogenes*	78.9% Amoxicillin, 73.1% tetracycline, and 81.8% trimethoprim/sulfamethoxazole	Human	Ivory Coast	Moroh et al. (2014)
Klebsiella oxytoca	64.5% MAR	Human	Libya	Mohammed et al. (2016)
Providencia rettgeri	63.2% MAR			
Pseudomonas aeruginosa	52.1% MAR			
Acinetobacter baumannii, *Citrobacter freundii,* and *Enterobacter aerogenes*	47.4% MAR			
Enterobacter amnigenus biogroup 2	42.1% MAR			
Enterobacter cloacae	(40.8%) MAR			
ESBL-producing Klebsiella pneumoniae strains	89% Trimethoprim–sulfamethoxazole, 89% gentamicin, 84% ciprofloxacin, and 50% amikacin	Human	Morocco	El Bouamri et al. (2015)

Key: *MAR* multiple antibiotic resistance and *ESBL* Extended-Spectrum Beta-Lactamase

animals including fish intended for human consumption in Nigeria (Oloso et al. 2018).

Consistent to the existence of ARB in fish from aquaculture and wild environments, their corresponding ARGs also have been detected in cultured fish from Tanzania (Shah et al. 2012) and wild fish from Tanzania (Moremi et al. 2016), Egypt (Ramadan et al. 2018), Algeria (Brahmi et al. 2018; Dib et al. 2018), and South Africa (Fri et al. 2018) (Table 8.2). Coherent to ARB, it is possible that the ARGs detected originate from the aquatic environment (Adesoji and Ogunjobi 2016; Lyimo et al. 2016; Stenstrom et al. 2016). In general, the human health risk

Table 8.2 Antibiotic resistance genes isolated from fish and other environments in Africa

Antibiotic resistance genes	Resistance to antibiotic	Sample isolated	Country	Reference
tetA(A) and *tetA(G)*	Tetracycline	Water, sediments, and fishpond	Tanzania	Shah et al. (2012)
sul1 and *sul2*	Sulfonamides			
intl1 and *int2*	Transfer of genes[a]			
dfrA1, dfrA7, dfrA12	Trimethoprim			
strA-strB	Streptomycin			
cat-1	Chloramphenicol			
bla_{TEM}	β-Lactam/amoxicillin			
mefA	Erythromycin			
sul1, sul2	Sulfonamides	Wild fish and water samples	Tanzania	Moremi et al. (2016)
tet(A), tet(B)	Tetracycline			
aac(6′)-Ib-cr, *qnr*S1	Fluoroquinolones			
aac(3)-lld, *str*B, *str*A	Aminoglycosides			
*dfr*A14	Trimethoprim			
$bla_{CTX\text{-}M\text{-}15}$	β-Lactams			
bla_{TEM}, $bla_{\mathrm{CTX\text{-}M}}$, bla_{CMY}, bla_{OXA}	β-Lactams	Fish from market	Egypt	Ramadan et al. (2018)
$bla_{\mathrm{CTX\text{-}M\text{-}15}}$	β-Lactams	Wild fish and shrimp	Algeria	Dib et al. (2018)
$bla_{\mathrm{CTX\text{-}M}}$	β-Lactams	Wild fish	Algeria	Brahmi et al. (2018)
oqxAB	Quinolones			
Qnr, aac(6′)-Ib-cr	Fluoroquinolones			
bla_{OXA}	β-Lactams	Wild fish and water from fish farms	South Africa	Fri et al. (2018)
Tet(A), tet(M)	Tetracycline			
sul1, sul2	Sulfonamides			
*dfr*1	Trimethoprim			
*erm*B	Macrolides, lincosamides, and streptogramin			
*str*A	Aminoglycosides			
nptII	Neomycin			
SXT integrase	Transfer of genes[a]			
Tet(A), tet(E) tet(B), tet(M), Tet39	Tetracycline	Treated and untreated water	Nigeria	Adesoji et al. (2015)
Tet(A), Tet(B)	Tetracycline	Drinking water sources	Tanzania	Lyimo et al. (2016)
$bla_{\mathrm{TEM\text{-}1}}$, $bla_{\mathrm{CTX\text{-}M}}$	β-Lactams			
bla_{TEM}, bla_{SHV}, bla_{CTX}	β-Lactams	Drinking water sources	Nigeria	Adesoji and Ogunjobi (2016)
blaAIM-1, blaGES-21	β-Lactams	Wastewater	Burkina Faso	Bougnom et al. (2019)
Enterobacteriaceae plasmid replicons	Transfer of genes[a]			

(continued)

Table 8.2 (continued)

Antibiotic resistance genes	Resistance to antibiotic	Sample isolated	Country	Reference
Tet(B), Tet(39)	Tetracycline	Freshwater and soil samples	South Africa	Stenstrom et al. (2016)
Sul 3	Sulfonamides	Rhizospheres plant	South Africa	Adegoke and Okoh (2015)
$bla_{\text{CTX-M}}$, bla_{TEM},	β-Lactams	Various foods	Egypt	Hammad et al. (2018)
tet(A), tet(E)	Tetracycline			
intI1	Transfer of genes[a]			
$bla_{\text{OXA-23}}$, $bla_{\text{OXA-51}}$	Carbapenems	Human	Senegal	Diene et al. (2013)

Key: *ESBL* Extended-Spectrum Beta-Lactamases

[a] Indicates transposons responsible for the transfer of ARGs

associated with ARGs is not only contributed by fish. Reasonably, ARGs have also been found in drinking water in Tanzania (Lyimo et al. 2016) and Nigeria (Adesoji et al. 2015; Adesoji and Ogunjobi 2016), Rhizospheres plants in South Africa (Adegoke and Okoh 2015), various foods in Egypt (Hammad et al. 2018), and wastewater used for urban agriculture in Burkina Faso (Bougnom et al. 2019). Accordingly, ARGs have been detected in the human body in Senegal (Diene et al. 2013).

Similar to ARB, the ARGs detected are those encoding resistance to common antibiotics used for the frequent treatment of human diseases in Africa. Thus, Africans are currently exposed to a double resistance to antibiotics due to the presence of ARB and ARGs. Indeed, transposons and plasmids for transfer of ARGs have been detected in wild fish and water from fish farms in Tanzania (Shah et al. 2012) and South Africa (Fri et al. 2018), various foods in Egypt (Hammad et al. 2018), and wastewater used for agriculture in Burkina Faso (Bougnom et al. 2019). Since antibiotics exist ubiquitously in the environment, Africans are exposed to high health risks due to their close interaction with livestock and the aquatic ecosystem (Wamala et al. 2018), which signifies increased morbidity and mortality (Gyansa-Lutterodt 2013) due to the failure of antibiotics to treat bacterial diseases. The obtained results emphasize the need for policies and mechanisms to limit the use of antibiotics in food animals production in order to protect human health. Moreover, physicians should devise some methods to change patients' treatment pattern depending on antibiotics susceptibility results. Antibiotics may also pose direct public health effects due to their residuals in different foods consumed by humans as detailed below.

8.4.2 Direct Potential Human Health Risk from Consumption of Fish

Globally, antibiotics residues in foods have attracted much attention in recent years because of growing food safety and public health concerns (Capita and Alonso-Calleja 2011; Landers et al. 2012; Berendonk et al. 2015). Their presence in food animals represent socioeconomic challenges in global trade and consumed animal products (Okocha et al. 2018). In most countries, the use of antibiotics for food animals production requires a withdrawal period before the product can be sold for human consumption. Despite this regulation, most antibiotics are used without observing such a regulation both in fish (Pham et al. 2015) and other animals (Mubito et al. 2014). Consequently, high levels of antibiotics exist in food animals intended for human consumption, which pose a direct human health risk.

Limited studies have been conducted in Africa to detect antibiotics residues in fish and other foods. In Nigeria, Olatoye and Basiru (2013) found oxytetracycline levels in cultured *C. gariepinus* in the liver and fillets exceeded the Codex Alimentarius Commission established maximum residue limit of 600 and 200 μg/kg, respectively (Table 8.3). Similarly, a study conducted by Olusola et al. (2012) in Nigeria also found tetracycline exceeded international limits of 200 μg/kg from fresh and frozen *C. gariepinus* and *O. niloticus,* while chloramphenicol, which has a zero tolerance level, was detected in Officers' Mess. It has been reported that, in

Table 8.3 Residues of antibiotics from fish and other environments in Africa

Antibiotic	Residue amount	Tissue/sample	Country	Reference
Oxytetracycline	875.32 ± 45 μg/kg	Fish liver	Nigeria	Olatoye and Basiru (2013)
	257.2 ± 133 μg/kg	Fish fillets		
Tetracycline	2185 ± 412 μg/kg	Fresh and frozen fish	Nigeria	Olusola et al. (2012)
Chloramphenicol	837 ± 165 μg/kg			
Ampicillin	0.36 ± 0.04 μg/L	WWTPs	Kenya	Kimosop et al. (2016)
	0.79 ± 0.07 μg/L	Hospital		
Sulfamethoxazole	1.8 μg/L	River water	Kenya	Ngumba et al. (2016)
Trimethoprim	0.327 μg/L			
Ciprofloxacin	0.129 μg/L			
Sulfamethoxazole	0.02–38.85 μg/L	River water	Kenya	K'Oreje et al. (2016)
Trimethoprim	0.05–6.95 μg/L			
Tetracycline	0.85 ± 0.06 μg/mL	Surface water	Nigeria	Olaniran et al. (2018)
	0.23 ± 0.01 μg/mL	Untreated effluent water		
Sulfamethoxazole	34.50 μg/L	WWTPs	South Africa	Matongo et al. (2015)
Oxytetracycline	785.58 ± 210.80 μg/L	Cow milk	Tanzania	Ridhiwani (2015)
Oxytetracycline	2604.1 ± 703.7 μg/kg	Cattle muscle	Tanzania	Kimera et al. (2015)
	3434.4 ± 606.4 μg/kg	Cattle liver		
	3533.1 ± 803.6 μg/kg	Cattle kidney		

Africa, as in other parts of the world, antibiotic residues in animal-derived foods more commonly exceed the world health organization (WHO) threshold residue levels (Darwish et al. 2013). This further highlights the high human health risk caused by antibiotics because they have also been detected in wastewater treatment plants (WWTPs) in Kenya (Kimosop et al. 2016) and South Africa (Matongo et al. 2015), surface water in Nigeria (Olaniran et al. 2018), hospitals (Kimosop et al. 2016) and river water (K'Oreje et al. 2016; Ngumba et al. 2016) in Kenya, cow's milk in Tanzania (Ridhiwani 2015) and Algeria (Layada et al. 2016), untreated effluent water from a cow market in Nigeria (Olaniran et al. 2018), and cattle muscle, liver, and kidney (Kimera et al. 2015) in Tanzania.

In practice, the human health risk resulting from antibiotics in Africa may be much higher because of multiple sources. Antibiotics are widely abused by humans for therapy, sometimes without physicians' prescription, and the quantity of antibiotics prescribed in African countries intended for the treatment of various diseases are high (Adegoke et al. 2018), contributing to elevated levels of residues. The antibiotic residues have been reported to spread rapidly, irrespective of geographical, economic, or legal differences in African countries (Darwish et al. 2013). This represents a serious concern because antibiotics, particularly chronic dietary oxytetracycline used in fish production, have been recently reported to cause direct human health risk in children (Limbu et al. 2018). In general, despite the existence of limited studies on antibiotics residues from cultured fish, the results obtained from *C. gariepinus* and *O. niloticus* suggest a widespread human health risk because the two fish species are widely consumed in African countries. Thus, there is an urgent need to control the use of antibiotics in fish intended for human consumption in order to protect human health.

8.5 Conclusion

It is clear that studies on antibiotics used in aquaculture production in Africa are still limited particularly on effects on fish anatomy and physiology. However, the existing limited data highlight toxic effects of antibiotics in the fish body and increasing prevalence of ARB and ARGs coupled with high residues of antibiotics in cultured fish, which pose a significant human health risk. The African countries require coordinated actions to tackle the indiscriminate use of antibiotics in humans, livestock, agriculture, and aquaculture at its grassroots, because currently most of them are characterized by inadequate monitoring, surveillance and weak regulatory systems. Clear policy directions for prohibiting the use of antibiotics on food animals production are urgently needed to protect human health. More studies should be conducted on the potential risks of antibiotics on fish and human health resulting from multiple exposure scenarios.

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